

Docket No.: PC-0044 CIP

**REMARKS**

The specification has been amended to correct inadvertent typographical and grammatical errors, and the claims have been amended to clarify the invention. The specification has been amended in the paragraph beginning at p. 3, line 15 to describe variants of the polynucleotides encoding the polypeptides of SEQ ID NOs:1-6, and in the paragraph beginning at p. 4, line 13 to describe variants of the polypeptides of SEQ ID NOs:1-6. Support for these amendments is found in the priority application, USSN 09/156,513 at p. 2, line 38 through p. 3, line 6. The specification has also been amended in the paragraph beginning at p. 1, line 3 to recite "USSN 09/156,513, filed 17 September 1998, now abandoned". The paragraph beginning at p. 10, line 26 has been amended to recite "Example VII", and the paragraph beginning at p. 11, line 13 has been amended to recite "the cDNA encoding the human protein". Claim 1 has been amended to recite specific fragments of SEQ ID NO:1 and to recite a variant of SEQ ID NO:1 having at least 90% amino acid sequence identity to SEQ ID NO:1, and the complements of the encoding polynucleotides. Claim 2 has been amended to recite a variant of SEQ ID NO:7 having at least 95% identity to the nucleic acid sequence of SEQ ID NO:7. Support for the amendments to claims 1 and 2 are found throughout the specification. For example, support for the amendment to claim 1 is found at p.11, lines 8-12 which recites specific fragments of SEQ ID NO:1 representing transmembrane domains characteristic of the GPCR receptor family, and in the paragraphs beginning at p. 3, line 15; p. 4, line 13; and p. 9, line 5 which describe variants of the polynucleotides and polypeptides of the invention. Support for the amendments to claim 2 is likewise found in the paragraphs described above, and further in the Table at p. 11 which describes specific variants of the polynucleotide sequence of SEQ ID NO:7. No new matter is added by any of these amendments, and entry of the amendments is requested..

**Priority**

The Examiner stated that this application filed under 37 CFR 1.60 lacks the current status of the nonprovisional parent application 09/516,513. The Examiner stated that a statement reading "(now abandoned)" should be included after "09/156,513, filed 17 September 1998" following the title. The application has been so amended.

**Specification**

The Examiner objected to the disclosure because at p. 10, line 26, the specification states that transcript imaging is shown in Example VIII while transcript imaging is shown in Example VII on pp. 34-37. Appropriate correction is required. The specification has been amended at p. 10, line 26 to recite Example VII. Withdrawal of the objection is therefore requested.

**Docket N .: PC-0044 CIP****35 U.S.C. §§ 101/112 Rejection of Claims 1-6**

The Examiner has rejected claims 1-6 under 35 U.S.C. §§ 101 and 112, first paragraph, because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility as determined according to the current Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001.

The Examiner stated that the instant specification discloses that the polypeptide comprising the amino acid sequence of SEQ ID NO:1 is presumably a member of the G-protein coupled receptor (GPCR) superfamily identified as a metabotropic GPCR, based on homology to that family of proteins. The Examiner stated that the specification describes methods of use of the proteins and nucleic acids of the invention such as in screening assays to identify ligands and binding compounds, methods to inhibit or regulate expression of the nucleic acid or polypeptide, use of the nucleic acids as probes to identify related genes, to produce a protein, etc. However, the Examiner stated, these are considered general methods applicable to any protein and/or nucleic acid and are not considered specific and substantial to the instant invention.

The Examiner stated that the nucleic acids, proteins, and associated antibodies and antisense nucleic acids can be used diagnostically to detect abnormal levels of the proteins or nucleic acids with associated disorders or diseases such as infection, inflammation, and cancer, and particularly meningioma of the brain. However, the Examiner stated, this utility is not specific or substantial, and is based on the fact that the cDNA encoding SEQ ID NO:1 was first identified from a brain meningioma cDNA library.

The Examiner stated that Applicants provide information from transcript images on pp. 34-37 in which cDNA libraries from different tissues were assayed for abundance of the nucleic acid of SEQ ID NO:7. See, in particular, the Table at p. 35, lines 10-16. However, the Examiner stated, it is not clear from the information in the specification how the numbers in the abundance and % abundance were derived, or what these numbers mean, so it is difficult to interpret their meanings. Applicants also state that the sequence was not expressed in cytologically normal thyroid (5 libraries), lymphocytic thyroiditis (2 libraries) hyperthyroidism, goiter or papillary carcinoma. The Examiner interpreted from this that the abundance in these libraries would be 1, as in the first and third libraries in the Table for SEQ ID NO:7. However, although applicants state that SEQ ID NO:7 is diagnostic for thyroid tumor and specifically follicular carcinoma, the increase in abundance was not seen with the first and third libraries in the comparison, which are from cancerous tumors. Also, the Examiner stated, the assertion that the sequence can be used diagnostically is based on the result from a single library and the skilled artisan

**Docket No.: PC-0044 CIP**

would not find it credible that this nucleic acid could be used diagnostically to detect follicular carcinoma based on a slight increase in expression of the gene from a single library. Finally, the Examiner stated, cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (Sen, 2000, Curr Opin Oncol 12:82-88) and the data was not corrected for this. A slight amplification of a gene does not necessarily mean overexpression in a cancer tissue, but can merely be an indication that the cancer is aneuploid.

**Applicants Response**

Applicants respectfully traverse the rejection and submit that the Examiner has not met his burden of proof to provide evidence or sound scientific reasoning why one skilled in the art would have reason to doubt Applicants assertion of utility. The Examiner is reminded that the utility requirement, according to established law, is not an onerous one.

To meet the utility requirement of sections 101 and 112 of the Patent Act, the patent applicant need only show that the claimed invention is "practically useful," *Anderson v. Natta*, 480 F.2d 1392, 1397, 178 USPQ 458 (CCPA 1973) and confers a "specific benefit" on the public. *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689 (1966). As discussed in a recent Court of Appeals for the Federal Circuit case, this threshold is not high:

An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. See *Brenner v. Manson*, 383 U.S. 519, 534 [148 USPQ 689] (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 [24 USPQ2d 1401] (Fed. Cir. 1992) ("to violate Section 101 the claimed device must be totally incapable of achieving a useful result"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is incapable of serving any beneficial end").

*Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999).

While an asserted utility must be described with specificity, the patent applicant need not demonstrate utility to a certainty. In *Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 USPQ2d 1094 (Fed. Cir. 1991), the United States Court of Appeals for the Federal Circuit explained:

An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding lack of utility." *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed. Cir. 1984).

The specificity requirement is not, therefore, an onerous one. If the asserted utility is described so that a person of ordinary skill in the art would understand how to use the claimed invention, it is sufficiently specific. See *Standard Oil Co. v. Montedison, S.p.a.*, 212 U.S.P.Q. 327, 343 (3d Cir. 1981). The specificity requirement is met unless the asserted utility amounts to a "nebulous expression"

**Docket No.: PC-0044 CIP**

such as "biological activity" or "biological properties" that does not convey meaningful information about the utility of what is being claimed. *Cross v. Iizuka*, 753 F.2d 1040, 1048 (Fed. Cir. 1985).

In addition to conferring a specific benefit on the public, the benefit must also be "substantial." *Brenner*, 383 U.S. at 534. A "substantial" utility is a practical, "real-world" utility. *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881 (CCPA 1980).

If persons of ordinary skill in the art would understand that there is a "well-established" utility for the claimed invention, the threshold is met automatically and the applicant need not make any showing to demonstrate utility. Manual of Patent Examination Procedure at § 706.03(a). Only if there is no "well-established" utility for the claimed invention must the applicant demonstrate the practical benefits of the invention. *Id.*

Once the patent applicant identifies a specific utility, the claimed invention is presumed to possess it. *In re Cortright*, 165 F.3d 1353, 1357, 49 USPQ2d 1464 (Fed. Cir. 1999); *In re Brana*, 51 F.3d 1560, 1566; 34 USPQ2d 1436 (Fed. Cir. 1995). In that case, the Patent Office bears the burden of demonstrating that a person of ordinary skill in the art would reasonably doubt that the asserted utility could be achieved by the claimed invention. *Id.* To do so, the Patent Office must provide evidence or sound scientific reasoning. See *In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). If and only if the Patent Office makes such a showing, the burden shifts to the applicant to provide rebuttal evidence that would convince the person of ordinary skill that there is sufficient proof of utility. *Brana*, 51 F.3d at 1566. The applicant need only prove a "substantial likelihood" of utility; certainty is not required. *Brenner*, 383 U.S. at 532.

The Examiner has not presented any evidence or sound scientific reasoning why one skilled in the art would doubt Applicant's identification of the disclosed polypeptide of SEQ ID NO:1 as a G-protein coupled receptor (GPCR) and, in particular, a member of the subfamily of metabotropic GPCRs having a well-established utility (see specification at p. 2, lines 11-21). The Examiner merely states that "SEQ ID NO:1 is presumably a member of the G-protein coupled receptor (GPCR) superfamily identified as a metabotropic GPCR based on homology to that family of proteins" but offers no evidence to refute this assertion. As noted above, in view of a well-established utility for the claimed invention based on this identification, the threshold for a specific and substantial utility is met automatically and the applicant need not make any showing to demonstrate utility.

In addition, however, applicants have presented ample evidence for an asserted utility of the claimed polynucleotide of SEQ ID NO:7 as diagnostic for cancer, in particular, follicular carcinoma of the

**Docket No.: PC-0044 CIP**

thyroid based on significant differential expression (4-fold) in that disease condition over that found in any other thyroid tissue examined, either normal or otherwise diseased. See specification at p. 35, lines 7-22. In this case the Examiner does give some reasons as to why one skilled in the art would doubt this assertion by applicants, but appears to misinterpret the data in the process. The Examiner first states that "it is not clear from the information in the specification how the numbers in the abundance and % abundance were derived, or what these numbers mean, so it is difficult to interpret their meanings". Applicants submit that one skilled in the art would understand that "Abundance" refers to the number of transcripts of the sequence in question found in the library, while "% Abundance" refers to the number of transcripts of the sequence in question relative to the total number of transcripts in that library. Since SEQ ID NO:7 was disclosed as not found in various other thyroid libraries unassociated with follicular carcinoma, e.g., 5 normal thyroid libraries and 2 lymphocytic libraries, this would mean that the abundance of the transcript in these libraries was "0", not "1" as the Examiner has interpreted. The relative abundance of the transcript in different libraries expressed as "% Abundance" is particularly significant because it is the relative abundance of the specific transcript compared with all RNA transcripts in the sample that determines the level of expression. Therefore, the finding of at least a 4-fold higher expression of this sequence in follicular carcinoma compared with any other thyroid tissues examined is highly significant and would provide a clear utility to one skilled in the art for the use of the polynucleotide in the detection and diagnosis of this condition in thyroid tissue exhibiting at least a 4-fold increase in expression relative to control samples.

The Examiner's contention that the occurrence of this transcript in only a single library associated with follicular carcinoma is not sufficient to support its' use as a diagnostic indicator for this condition is also not supported by any evidence or sound scientific reasoning. The fact that a number of thyroid libraries were examined representing both normal and diseased thyroid, and that only the library associated with follicular carcinoma showed a level of expression 4-fold higher than any other thyroid tissue clearly indicates that, more likely than not, the level of expression of the gene transcript in this tissue is associated with the disease condition. This likelihood is further supported by the fact that the next most abundant expression of the gene transcript was found in a library associated with follicular "adenoma" (THYRNOT03), a benign, precancerous condition to follicular carcinoma. Thus it is presumptuous to conclude that one skilled in the art would not consider the significance of these findings in considering the credibility of applicants asserted use of the polynucleotide in the detection and diagnosis of follicular carcinoma of the thyroid.

**Docket No.: PC-0044 CIP**

Finally, the Examiner contends that the "slight" amplification of the gene transcript in follicular carcinoma may be simply due to aneuploidy, an abnormal number of chromosomes in cancerous tissue, and that the data must somehow be corrected for this possibility. Again, however, the Examiner offers no suggestion why this must be done, how it may be done, or whether it is common in the art for such a correction to be made in using differential expression of a gene as a diagnostic tool for cancer detection. The reference cited by the Examiner (Sen, 2000, Curr Opin Oncol, 12:82-88) makes no such suggestion and, in fact, teaches that aneuploidy may be a useful diagnostic tool for risk assessment and prognosis for certain cancers. See, in particular, pp. 83-84 of Sen. Further, the Sen article teaches that aneuploidy and chromosomal instability may differ according to different cancer types. In thyroid cancers in particular, the only reference to aneuploidy in follicular carcinomas suggests that "Genome wide screening of follicular thyroid tumors revealed frequent loss of chromosome 22 in widely invasive follicular carcinomas" (p. 84, second column). Thus, the only evidence of aneuploidy in follicular carcinomas would not account for the increased expression of a gene associated with the disease as disclosed in the instant application.

In conclusion, applicants submit that the Examiner has not met the necessary burden of proof in providing evidence or sound scientific reasoning why one skilled in the art would doubt either that a well established utility exists for the claimed invention, or that applicant's asserted use of the claimed invention in the detection and diagnosis of follicular carcinoma of the thyroid could be achieved without further undue experimentation. Applicants therefore respectfully request withdrawal of the rejection of claims 1-6 under 35 U.S.C. § 101. Applicants further submit that to the extent the claims are likewise rejected under 35 U.S.C. § 112, first paragraph, because one skilled in the art clearly would not know how to use the claimed invention for the reasons set forth by the Examiner above, this rejection is likewise unsubstantiated and should be withdrawn.

35 U.S.C. § 112, Second Paragraph, Rejection of Claims 1 and 3-6

The Examiner has rejected claims 1 and 3-6 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner stated that claim 1 encompasses a cDNA encoding a nucleic acid encoding a protein and the complement thereof. The Examiner stated, however that a cDNA is double stranded and therefore already includes the complement of the encoding strand.

Applicants submit that claim 1 recites "An isolated cDNA comprising a nucleic acid encoding an amino acid sequence selected from...". Since the complement of the cDNA encoding the recited amino

**Docket No.: PC-0044 CIP**

acid sequences of elements a) and b) would not encode the same amino acid sequences, it necessary and appropriate to specifically recite "the complement of the encoding nucleic acid sequence of a) or b)" as recited in element c) to be clear and definite. Applicants therefore request withdrawal of the rejection of claims 1 and 3-6 under 35 U.S.C. § 112, second paragraph.

**35 U.S.C. § 102(b), Rejection of Claims 1 and 3-6**

The Examiner has rejected claims 1 and 3-6 under 35 U.S.C. § 102(b) as anticipated by Valenzuela et al., WO 99/55721, Nov. 4, 1999. Applicant is advised that the instant application can only receive the benefit under 35 U.S.C. § 120 from an earlier filed application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention. Because the instant application does not meet the requirements of 35 U.S.C. § 112, first paragraph, for the reasons given above, and it is a continuation of application Serial No. 09/516,513, the prior application does not meet these requirements and therefore is unavailable under 35 U.S.C. § 120. Valenzuela disclose a nucleic acid molecule (SEQ ID NO:43, claim 52) that encodes a protein (SEQ ID NO:45, claim 53) that is 100% identical to the polypeptide of SEQ ID NO:7 of the instant application, thus anticipating the claims.

Applicants submit that, for the reasons discussed above, the present application meets the requirements for 35 U.S.C. § 112, first paragraph with respect to the claimed invention and that, as a continuation of application Serial No. 09/516,513, the prior application likewise meets these requirements with respect to the same claimed invention. Therefore the requirements for 35 U.S.C. § 120 for claiming the benefit of the earlier filed application are met, and Valenzuela et al. therefore do not anticipate the claimed invention. Withdrawal of the rejection of claims under 35 U.S.C. § 102(b) is therefore requested.

Docket No.: PC-0044 CIP

**CONCLUSION**

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections and rejections. Early notice to that effect is earnestly solicited. Applicants further submit that upon allowance of claim 1, that claims 7-12 be rejoined and examined as methods of use of the polynucleotides of claim 1 that depend from and are of the same scope, in accordance with *In re Ochiai and Brouwer* and the MPEP § 1801.04.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Agent of record, below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. 09-0108.

Respectfully submitted,

INCYTE GENOMICS, INC.

Date:

January 14, 2003David G. Streeter, Ph.D.

David G. Streeter, Ph.D.

Reg. No. 43,168

Direct Dial Telephone: (650) 845-5741

3160 Porter Drive  
Palo Alto, California 94304  
Phone: (650) 855-0555  
Fax: (650) 849-8886



Docket No.: PC-0044 CIP

**VERSION WITH MARKINGS TO SHOW CHANGES MADE****IN THE SPECIFICATION:**

The paragraph beginning at line 3 of page 1 has been amended as follows:

This application is a continuation-in-part of USSN 09/156,513, filed 17 September 1998, now abandoned.

The paragraph beginning at line 15 of page 3 has been amended as follows:

The invention provides an isolated cDNA comprising a nucleic acid sequence encoding a protein having the amino acid sequence of SEQ ID NOs:1-6. The invention further provides an isolated and purified polynucleotide variant having at least 70% polynucleotide sequence identity to the polynucleotide encoding the polypeptide selected from the group consisting of SEQ ID NOs:1-6. The invention also provides an isolated cDNA selected from a nucleic acid sequence of SEQ ID NOs:7-12, fragments of SEQ ID NOs:7-12 selected from SEQ ID NOs:13-52, and variants of SEQ ID NOs:7-12 selected from SEQ ID NOs:53-74 and the complements of SEQ ID NOs:7-74. The invention additionally provides compositions, a substrate, and a probe comprising the cDNA or the complement of the cDNA. The invention further provides a vector comprising the cDNA, a host cell comprising the vector and a method for making a protein comprising culturing a host under conditions to produce the protein and recovering the protein from culture. The invention still further provides a transgenic cell line or organism comprising the vector containing the cDNA encoding a GPCR. The invention additionally provides a fragment, a variant, or the complement of a cDNA selected from SEQ ID NOs:13-74. In one aspect, the invention provides a substrate containing at least one nucleotide sequence selected from SEQ ID NOs:7-74 or the complements thereof. In a second aspect, the invention provides a probe comprising a cDNA or the complement thereof which can be used in methods of detection, screening, and purification. In a further aspect, the probe is selected from a single-stranded RNA or DNA molecule, a peptide nucleic acid, a branched nucleic acid and the like.

The paragraph beginning at line 13 of page 4 has been amended as follows:

The invention provides a purified protein or a portion thereof selected from the group consisting of an amino acid sequence of SEQ ID NOs:1-6, a variant of SEQ ID NOs:1-6 having at least 90% amino acid sequence identity to SEQ ID NOs:1-6, an antigenic epitope of SEQ ID NOs:1-6, and a biologically active portion of SEQ ID NOs:1-6. The invention also provides a composition comprising the purified protein and a pharmaceutical carrier. The invention further provides a method of using a GPCR to treat a

**Docket No.: PC-0044 CIP**

subject with infection, inflammation or cancer comprising administering to a patient in need of such treatment the composition containing the purified protein or a portion thereof. The invention still further provides a method for using a protein to screen a library or a plurality of molecules or compounds to identify at least one ligand, the method comprising combining the protein with the molecules or compounds under conditions to allow specific binding and detecting specific binding, thereby identifying a ligand which specifically binds the protein. In one aspect, the molecules or compounds are selected from DNA molecules, RNA molecules, peptide nucleic acids, peptides, proteins, mimetics, agonists, antagonists, antibodies, immunoglobulins, inhibitors, and drugs. In another aspect, the ligand is used to treat a subject with infection, inflammation and cancer, particularly meningioma of the brain.

The paragraph beginning at line 26 of page 10 has been amended as follows:

Transcript imaging as shown in Example VII [VIII] details the specific and differential expression of SEQ ID NOs:7-12 in human disorders. In particular, the transcript images show that the nucleic acid sequence, protein or an antibody specific for the protein can be used in diagnostic assay for the following disorders:

The paragraph beginning at line 13 of page 11 has been amended as follows:

Mammalian variants of the cDNAs encoding the GPCRs were identified using BLAST2 with default parameters and the ZOOSEQ databases (Incyte Genomics, Palo Alto CA). These preferred variants have from about 84% to about 95% [amino acid] sequence identity to the cDNA encoding the human protein as shown in the table below. The first column shows the SEQ ID<sub>H</sub> for the human cDNA; the second column, the SEQ ID<sub>VAR</sub> for variant cDNAs; the third column, the clone numbers for the variants; the fourth column, the species; the fifth column, percent identity to the human cDNA; and the six column, the nucleotide alignment (Nt<sub>H</sub>) of the human and variant cDNAs

**IN THE CLAIMS:**

Claims 1 and 2 have been amended as follows:

1. (Twice Amended) An isolated cDNA comprising a nucleic acid encoding an [the] amino acid sequence selected from:

a) an amino acid sequence of SEQ ID NO:1;

b) a fragment of SEQ ID NO:1 from I51-V72, G88-V109, C116-A145, I156-L175, M207-P229, or G242-T264 of SEQ ID NO:1;

Jun. 4. 2003 9:19AM

INCYTE LEGAL DEPT

No. 7961 P. 1/20

*7/24/03*  
 *DATE 7-14-03*  
*Official Fax* *6/4/03*  
*EPA*

Incyte Corporation  
Legal Department  
3160 Porter Drive  
Palo Alto, CA 94304  
Telephone: (650) 855-0555  
Facsimile: (650) 845-4166  
(650) 849-8886

Date: June 4, 2003  
To: Examiner O'Hara  
Company: USPTO  
Fax No.: 703-746-6901  
Telephone No.: 703-308-3312  
From: David Streeter  
Our Ref. No.: PC-0044 CIP  
Your Ref. No.: 09/895,686  
Page(s): 20 , including cover sheet

Comments:

Per our discussion, enclosed herewith please find the Response to Office Action filed on January 14, 2003, along with a copy of the mail log affirming the filing of the Response on that day.

This facsimile is intended for the addressee only and may contain confidential information. If you have received this facsimile in error, please call us at 650.855.0555 immediately to arrange for its return.

Received from <415 852 0195> at 6/4/03 1:26:40 PM [Eastern Daylight Time]

DATE	FILE #	EXPRESS #	INITIALS
1/10/03	PC-0011 CIP	FC	mm lt
1/13/02	PF-0675 USN	FC	KS
1/13/03	PF-1641P	EL 947441362 US	KS
1/13/03	PF-1655P	EL 947441376 US	KS
1/13/03	PF-1654P	EL 856167618 US	KS
1/13/03	PB-0006 CIP	FAX	mm lt
	Related on 1/14/03		mm lt
1/14/03	PC-0044 CIP	FC	mm lt
1/14/03	PF-0069-10W	FC	die
1/14/03	PF-0638-20IU	FC	die
1/14/03	PF-0412-10IU	FC	die
1/15/03	PF-0446-10IU	FC	die
1/15/03	PF-1649 P	EL 947441331 US	KS
1/15/03	PF-1656 P	EL 947441359 US	KS
1/15/03	PF-0162 USN	EL 936657626 US	die
1/17/03	PF-0420-20IU	FC	die
1/17/03	PF-1650 P	EL 950616965 US	die
1/21/03	PC-0011-1 COM	EL 954507753 US	mm lt
1/21/03	PI-0245-USN	EL 954509581 US	mm lt
1/21/03	PF-0434-10IU	FC	mm lt
1/21/03	PV-0002 PCT	EV 211257348 US	Ague,
1/21/03	PF-1652 P	EV 183480751 US	Ague
1/21/03	PD-1028-1 CPA	FC	die
1/21/03	PD-1028-2 CON	EL 936657609 US	die
1/21/03	PF-0195-2 RCE	EL 947441328 US	KS
1/21/03	PI-0032 USN	FC	KS

\*

Jun. 4. 2003 9:19AM

INCYTE LEGAL DEPT

No. 7961 P. 3/20

Commissioner for Patents  
Box Non-Fee Amendment  
Washington, D.C. 20231

Mailed: 1/14/03  
Docket No. PC-0044 CIP

Applicants: Bandman et al.  
Serial No.: 09/895,686  
Filing Date: June 28, 2001  
Title: HUMAN GPCR PROTEINS

Enclosed are the following:

1. Return Postcard;
2. Transmittal Fee Sheet (1 pg., in duplicate); and
3. Response to Office Action (16 pp.)

DS/mmh

Method of Payment: Deposit Account

Docket No.: PC-0044 CIP

Certificate of Mailing

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Box Non-Fee Amendment, Commissioner for Patents, Washington, D.C. 20231 on 1/14/03.

By Margaret M. Hasson Printed: Margaret M. Hasson

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Bandman et al.

Title: HUMAN GPCR PROTEINS

Serial No.: 09/895,686

Filing Date: June 28, 2001

Examiner: O'Hara, E.

Group Art Unit: 1646

Box Non-Fee Amendment  
Commissioner for Patents  
Washington, D.C. 20231

TRANSMITTAL FEE SHEET

Sir:

Transmitted herewith are the following for the above-identified application:

1. Return Receipt Postcard; and
2. Response to Office Action (16 pp.).

The fee has been calculated as follows:

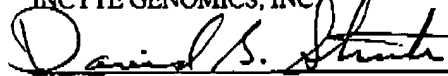
Claims	Claims After Amendment	-	Claims Previously Paid For	=	Present Extra	Other Than Small Entity Rate	Fee	Additional Fee(s)
Total	18	-	18	-	0	x\$18.00	0	\$ 0
Indept.	2	-	2	-	0	x\$84.00	0	\$ 0
First Presentation of Multiple Dependent Claims:						+280.00	0	\$ 0
Total Fee:								\$ 0

X No additional Fee is required.

The Commissioner is hereby authorized to charge any additional fees required under 37 CFR 1.16 and 1.17, or credit overpayment to Deposit Account No. 09-0108. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

INCYTE GENOMICS, INC



David G. Streeter, Ph.D.

Reg. No. 43,168

Direct Dial Telephone: (650) 845-5741

Date: January 14, 2003

Customer No.: 27904  
3160 Porter Drive  
Palo Alto, California 94304  
Phone: (650) 855-0555  
Fax: (650) 845-4166

105054

1

09/895,686